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ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/812,731	LIEW, CHOONG-CHIN	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *61 and 70-93* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *61 and 70-93* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is written in response to papers received 7/2/07. Claims 61 and 70-93 are pending and addressed in this office action.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 61 and 70-93 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Nature of the invention

The invention is drawn to a method detecting schizophrenia in a human test subject. The claims all include a step of determining the level RNA encoded by a BTG family, member2 (BTG2) gene in a blood sample obtained from said human and comparing the level with a quantified level of RNA encoded by said gene in blood samples from control subjects having schizophrenia, and wherein determination in step (b) of a statisticially significant similarity between said quantified level of RNA in blood from said control subjects is indicative of schizophrenia in said human test subject. Some claims additionally include a comparison with a

quantified level of RNA encoded by said gene in blood samples from control subjects that are healthy control subjects and/or control subjects not having said schizophrenia.

Some claims set additionally forth that a determination of a statistically difference between the test level and a quantified level of RNA from control subjects not having said schizophrenia and significant similarity between the test level and the level of control subjects having said schizophrenia "is indicative of said schizophrenia."

Some claims set additionally forth that a determination of a statistically difference between the test level and a quantified level of RNA from healthy control subjects and significant similarity between the test level and the level of control subjects having said schizophrenia "is indicative of said schizophrenia."

The nature of the invention requires the knowledge of a reliable association between comparing BTG2 expression and the indication that schizophrenia is present in a human. Further, the practice of the invention requires an understanding of how the presence of schizophrenia effects the level of BTG2 expression in human blood.

Further, the practice of the invention requires an understanding of how the presence of schizophrenia effects the level of BTG2 expression in human blood in patients having schizophrenia versus patients that do not have schizophrenia but may have some other disorders.

Scope of the claims

Some of the claims are broad with regard to the "control subjects not having schizophrenia" which would could encompass patients healthy patients, patients with some other disease, such as depression or rheumatoid arthritis or multiple sclerosis. .

The claims do not recite the level of statistical significance that is required to be reached, and so even with the requirement of statistical significance, the claims remain quite broad since no particular level is required. The phrase "statistically significant" describes a mathematical measure of a difference between groups, not a particular level of that difference which is acceptable. There is no universal accepted level of "statistically significant."

The claims are very broad in scope because they encompass that ANY level and direction of difference in gene expression between the healthy controls or the controls not having schizophrenia is indicative of said schizophrenia, if that difference is "statistically significant." That is, the claims do not set forth that one level should be higher or lower than the other, and further do not set forth how much of a "difference" between two individuals would be necessary to draw the conclusions set forth in the claims.

Teachings in the Specification/Examples

Regarding schizophrenia, the specification provides example 27 wherein gene expression profiles of blood samples from individuals having schizophrenia were compared with normal individuals, that is healthy patients. The specification teaches that 1,952 genes were identified as being differentially expressed, and regarding the instant claims, table 3Y provides a list of these genes (Example 27). BTG2 is among the genes.

Table 3Y teaches that the ratio of expression in schizophrenic samples relative to control samples is 2.46, indicating that in the tested samples, BTG2 was expressed, on average at a 2.46 times higher level in schizophrenic patients versus healthy controls. Table 3Y teaches that this result is significant p=0.0076.

The specification further provides example 51 which compares gene expression in patients having schizophrenia versus patients having manic depression syndrome. The specification teaches that 294 genes were identified as being differentially expressed, and regarding the instant claims, table 3AC provides a list of these genes (Example 51). BTG2 is among the genes. The table teaches that there is a p-value of 0.0013 for BTG2 expression, but the specification does not provide any guidance as to the level of "difference" between expression in the two populations, nor does the specification provide any guidance as to the direction of the difference (higher or lower expression) that is expected to be observed for any single pairing of samples.

Many of the claims are limited to a case where the control subjects do not have schizophrenia, but they could still have any other possible disease or condition. For example, the claims are inclusive of control subjects that have manic depression syndrome. For this embodiment of the claims, the specification does not provide information about an essential aspect of the invention, namely, the nature of the difference in expression that was observed between schizophrenia patients and manic depression syndrome patients.

Furthermore, though the specification teaches that this gene is differentially expressed in schizophrenia patients versus healthy patients, the specification teaches this is true for thousands of genes. There is no guidance or analysis of data in the specification to suggest that this gene in particular is sufficient to conclude that schizophrenia is present in a sample, as is instantly claimed. This information is essential to understanding and practicing the claimed invention because it is critical to knowing how to interpret a particular comparison result.

State of the Prior Art and Level of Unpredictability

Observing differences in expression between two populations is a highly unpredictable endeavor. While the instant specification teaches that BTG2 is differentially expressed in a population of schizophrenia patients versus control subjects, and even in a population of schizophrenia patients and manic depression disorder subjects, the specification does not establish that any particular level of expression of BTG2 (relative level or raw level) is sufficient to DETECT schizophrenia to the exclusion of other disorders, which is encompassed by the instant claims, and indeed, suggested by the instant claims.

Dangond et al. (US 2004/0018522) teach that BTG2 is differentially expressed in blood of patients with MS versus a group of controls that included healthy patients and patients with ALS (See examples, Tables 3, 6, 8, and 10). Pittman et al. teach that BTG2 is upregulated 2.15 fold in the blood of patients with rheumatoid arthritis versus healthy controls. These diseases are very different from schizophrenia, yet they display a similar expression phenotype- that is upregulation of BTG2 in blood samples from patients with illness versus healthy controls. This exemplifies that it is highly unpredictable whether or not one can conclude, simply from a blood sample of a test patient, that schizophrenia is present, since increased expression of the gene in blood could indicate some other disorder or phenotype is present, whether that is MS, rheumatoid arthritis or some other disease which has not yet been analyzed.

Iwamoto et al. teach that expression profiling in psychiatric fields have been notoriously discordant, with different studies often reporting conflicting gene expression data (The Neuroscientist, Vol. 12, Number 4, 2006, pages 349-361; Abstract and page 351). Tsuang et al. undertake an analysis that is very similar to the one in the instant specification. Regarding their

results, Tsuang et al. caution that the results must be interpreted with caution given several limitations including small sample size, the fact that the findings are not replicated in a separate cohort and results "may represent chance findings and type-I inferential errors," and that the patients tested were all on drugs that were not accounted for in the analysis (American Journal of Medical Genetics, Part B (Neuropsychiatric Genetics) 133B:1-5(2005)). All of these cautions set forth by Tsuang et al. appear to be equally relevant to the study set forth in the instant application. Vawter et al. teach that there is lack of consistency in the study of genes differentially expressed in schizophrenia which might be related to etiological and genetic heterogeneity of the illness (p. 42, Vawter et al. Schizophrenia Research, Vol. 67, pages 41-52, 2004). Further, Vawter et al. teach that genes that are significant by a t-test may not exceed the threshold for fold of change to be considered above background expression (p. 46). All of these taken together underscore and highlight the very unpredictable nature of this technology area.

Furthermore, although BTG2 was not observed to be differentially expressed in any of the other examples in this specification, it is unknown and unpredictable whether it would be expressed in the blood of patients having other mental illnesses or any other diseases which were not tested in the instant specification or diseases which were tested in the instant specification but in a different population of test subjects, and whether this expression would be different from levels of expression in healthy controls. It is unpredictable whether the gene is differentially expressed, for example, in patients having manic depression disorder versus healthy controls, and if it is, how this relates to the difference in expression between patients with schizophrenia and manic depression disorder. A method for detection which relies on a comparison between expression in the blood of a test subject and control subjects requires the knowledge of this

information in order to reliably "detect" schizophrenia, as set forth in the claims. The instant specification has not established that all difference, no matter the magnitude nor the direction, relative to any control subjects or even relative to a healthy control subject is indicative of schizophrenia. Furthermore, the specification has not shown that all expression at a level statistically the same as that observed in a population of patients having schizophrenia is sufficient to conclude that schizophrenia is present. In fact, as previously noted, Pittman et al. and Dangond et al. observed that this gene is over expressed in different diseases with highly dissimilar etiologies. It is entirely unpredictable if this is also the case with other diseases. It is not known under what circumstances the result observed in the instantly examined control and test populations would be repeatable, as the results have not been validated. But even if one were to obtain the same result in a comparison to patients with manic depression syndrome, for example, it would be unknown because applicant did not disclose the magnitude of difference in expression between schizophrenic populations and manic depression populations, nor did applicant disclose the direction of variation. All of these inquiries are particularly important in this case since the claims are silent as to which differential expression observations would be sufficient to detect the presence of schizophrenia.

Further, the claims of the instant application set forth the comparison of the gene expression in a single individual versus as few as one or two other individuals, and they set forth that a comparing gene expression between the two is "indicative of" schizophrenia. Neither the specification nor the claims set forth a threshold of difference between an individual's expression and the control expression of BTG2 in the blood that would be sufficient to conclude that the difference in gene expression between a test individual and any type control group is "indicative

of" the recited schizophrenia. Because the claims encompass any level of altered gene expression, it is relevant to point out that the art of Cheung et al (2003) teaches that there is natural variation in gene expression among different individuals. The reference teaches an assessment of natural variation of gene expression in lymphoblastoid cells in humans, and analyzes the variation of expression data among individuals and within individuals (replicates) (p.422, last paragraph; Fig 1). The data indicates that, for example, expression of ACTG2 in 35 individuals varied by a factor of 17; and that in expression of the 40 genes with the highest variance ratios, the highest and lowest values differed by a factor of 2.4 or greater (Fig 3). It is thus unpredictable as to whether or not any level of altered gene expression is indicative of a schizophrenia or the absence of schizophrenia.

The unpredictability of correlating gene expression level to any phenotypic quality is taught in the post-filing art of Wu (2001). Wu teaches that gene expression data, such as microarray data, must be interpreted in the context of other biological knowledge, involving various types of 'post genomics' informatics, including gene networks, gene pathways, and gene ontologies (p.53, left col.). The reference indicates that many factors may be influential to the outcome of data analysis, and teaches that expression data can be interpreted in many ways. The conclusions that can be drawn from a given set of data depend heavily on the particular choice of data analysis. Much of the data analysis depends on such low-level considerations as normalization and such basic assumptions as normality (p.63 - Discussion). The art of Newton et al (2001) further teaches the difficulty in applying gene expression results. Newton et al. teaches that a basic statistical problem is determining when the measured differential expression

is likely to reflect a real biological shift in gene expression, and replication of data is critical to validation (p.38, third full paragraph). There is no replication of data in the instant specification.

Quantity of Experimentation

The instant specification does not provide enabling support for the practice of a single embodiment within the claimed invention since the claimed invention results in the detection of schizophrenia. In particular, the specification does not provide adequate guidance to appraise one of ordinary skill in the art as to what levels of BTG2 gene expression must be observed to successfully conclude that schizophrenia is present. Further, although the specification teaches there are differences in BTG2 levels in a schizophrenia population versus a control patient population, and the specification teaches that for this population the difference is a 2.46 fold increase, the specification does not support the assertion in the claims that observing such an increase relative to any and all control populations of 2 or more individual is sufficient to "detect" schizophrenia. Thus, given the lack of teaching in the specification and the highly unpredictable nature of the technology, an extensive amount of work would be required to practice the claimed invention.

In order to practice the claimed invention, one would have to undertake an extensive amount of experimentation in a highly unpredictable technology area. One would have to begin by validating the results observed in the instant specification in a separate population of healthy and schizophrenic patients, in view of the established level of unpredictability in this technology area. One would have to further complete similar analysis for other diseases and conditions and control populations versus healthy controls and versus schizophrenic controls in order to attempt to establish when and if analysis of BTG2 expression is sufficient to conclusively detect

schizophrenia. For example, consider the comparison of a test result and a control population of individuals with manic depression How different from the average level of expression of healthy individuals would the test result have to be to indicate schizophrenia? Would any difference, up or down regulation be indicative of schizophrenia? Or could one result indicate schizophrenia and one a different disease such as MS or RA? Is BTG2 expressed in the blood of individuals with a disease other than schizophrenia, manic depression disorder, rheumatoid arthritis, and multiple sclerosis? Is this expression also diagnostic of other mental illnesses or other disorders entirely unrelated to schizophrenia? In order to reliably use a method for detecting schizophrenia, one would first have to answer at least these questions. One would also, however, have to carry out this testing for validation, for it is possible that the result observed in the instant specification is intrinsic to the cohort of patients evaluated in applicant's study. Further, one would have to undertake experimentation to determine difference thresholds required to determine that a patient has or does not have a disease.

As discussed, this art area is highly unpredictable.

Conclusion

The claims include methods which encompass the detection in blood of the expression of BTG2 in a test subject and comparing this expression to control subjects, wherein the comparison itself "is indicative of schizophrenia." The identification of gene differential expression/disease indication relationships is a highly unpredictable endeavor, requiring extensive experimentation. The specification provides minimal guidance. In light of the factors discussed, therefore, it is concluded that it would require undue experimentation to practice the claimed invention.

Response to Remarks

The rejections have been modified to address the amended claims and to address the newly added claims.

Applicant states that in view of the amendments "control subjects" does not necessarily encompass patients healthy patients or patients with some other disease, such as depression, rheumatoid arthritis or multiple sclerosis (p. 11 of response). This is true for claims that recite that the control patients have schizophrenia or are healthy control patients. But, it is not accurate for claims that recite that the "control patients do not have schizophrenia" as these control patients could be patients with depression, rheumatoid arthritis, multiple sclerosis or any other disease.

Applicant states in their summary of the nature of the invention and the scope of the claims that the claimed methods "do not permit 'any level and direction of difference in gene expression to be indicative of disease (p. 12 of response).'" The claims have been amended to require that statistically significant similarity between the test and control subjects having said schizophrenia, and in some also cases statistically significant difference between the test subject level and controls not having said bladder cancer schizophrenia or healthy controls, but still the claims are sufficiently broad so as to encompass any level or direction of difference, for the claims that recite the difference, provided the level rises to the level of "statistically significant." Further, the claims do not recite the level of statistical significance that is required to be reached, and so even with the requirement of statistical significance, the claims remain quite broad since no particular level of significance is required.

Applicant points out that the specification teaches that BTG2 RNA is expressed on average 2.46 fold greater than the level of expression of BTG2 RNA in healthy control patients ($p=0.0076$). This teaching in the specification is not commensurate in scope with the claims which set forth that schizophrenia can be detected, in some cases, simply by finding one individual as a "statistically similar" level of expression as another single individual who has schizophrenia. The detected level can be any level of expression. Furthermore, the rejection discusses a number of additional factors that result in the claimed invention lacking enablement even in view of this disclosure (for example the high level of unpredictability in this technology area and the fact that this gene is also upregulated in other diseases).

Applicant argues that the difference in direction and/or the fold change difference does not need to be included as a claim limitation to enable the invention because it does not require undue experimentation for one of skill in the art to measure a population of individuals having schizophrenia and determine what constitutes a statistically significant difference or similarity by following the methods disclosed in the specification (page 13 of response). However, this is not persuasive in view of the highly unpredictable nature of the invention as discussed in the rejection. Further, simply establishing that one has the same level of expression as a particular control group of patients "having said schizophrenia" is not sufficient to enable on to "detect" schizophrenia, as the claims set forth. The rejection discusses that this particular gene is also differentially expressed relative to different diseases, and in both cases the effect of disease is up regulation relative to healthy control samples. The claims recite that they are methods for "**detecting**" bladder cancer, and so in order to detect the disease one must be able to put the result into a larger context.

Applicant further argues on page 13 of the response that it does not require undue experimentation to determine the inherent direction or level of the statistically significant differential expression required, give the widely established and validated analytical tools for analyzing gene expression levels. This attorney argument is not supported by evidence on the record, for example showing an independent confirmation of the result given in the specification. The rejection discusses at length the art established need for replication in order to enable the use or a gene expression marker as a diagnostic tool, and indeed cites a post filing date reference where this is suggested for the gene that is the subject of the claimed invention. In the background of the unpredictable nature of the claimed invention, the lack of disclosure regarding the direction of the expression change and the level of the difference in bladder cancers and other diseases weighs heavily in the factors for determining that the claimed invention would require undue experimentation to practice.

Applicant states that the fact that it is disclosed that BTG2 is also differentially expressed in the schizophrenic population relative to those with manic depression is not detrimental to the value or enablement of the claimed invention since a difference between the two would be observed even if the control population were made up solely of manic depression patients (page 14). However, as discussed in the rejection, this result has not been validated in another population, and while the instant specification teaches that BTG2 is differentially expressed in a population of schizophrenia patients and manic depression disorder subjects, the specification does not establish that any particular level of expression of BTG2 (relative level or raw level) is sufficient to DETECT schizophrenia to the exclusion of other disorders, which is encompassed by the instant claims, and indeed, suggested by the instant claims.

Applicant states on page 15 that the claims do not require that BTG2 be sufficient to detect schizophrenia to the exclusion of all other disorders, stating that the use of a biomarker as an indication of disease is typically just one aspect of a multi-factorial process used for diagnosing the patient with the disease. However, this argument is not reflected in the claimed invention which positively sets forth in the preamble of the claim that the method is for DETECTING schizophrenia. Applicant undertakes a discussion of the meaning of "indication" pointing out that it is not equated with "diagnosis." The instant claims set forth that they are a method for detecting bladder cancer. Broadly and reasonable interpreted, "detecting a bladder cancer" means determining that it is there, and so the claims must be so enabled.

Applicant states that Pittman et al. nor Dangond et al. demonstrate that there is a statistically significant similarity in the levels of expression of BTG1 in schizophrenia and in the patients they tested (p. 16 of response). They did not attempt to make this showing. However, in view of their showings, prior to the practice of the claimed invention this is one of many unpredictable endeavors that would have to be carried out.

Applicant points out that Pittman et al. used fractionated blood samples and it is not known what the level of difference in expression would be in whole blood when comparing rheumatoid arthritis to control individuals (p. 16 of response). However, in view of their showings, prior to the practice of the claimed invention this is one of many unpredictable endeavors that would have to be carried out. Further, it is noted that many of the claims are inclusive of using detection of RNA in fractionated samples provided the detection is from a blood sample of the individual or the control subjects, so in some cases this argument is not even commensurate in scope with the instantly claimed invention (see claim 61, for example).

Applicant states that at worst the showings of the cited references would result in the BTG2 biomarker having reduced specificity (p. 17 of response). Again, applicant is reminded that the claims are for detecting the presence of disease, and this requires specificity to enable the claims as written.

Applicant points out that neither Iwamoto et al., Tsuang et al. nor Vawter et al. contradict the relevant teachings of the specification. These references are not cited to contradict the teachings of the specification, but instead to illustrate the highly unpredictable nature of the technology area. The examiner is not stating that the results obtained in the instant specification are invalid. The technology area of this invention is highly unpredictable, with often discordant results being observed. The instantly disclosed results have not been validated, and as discussed by Tsuang et al. these results must be interpreted with caution. The results have not been validated in an external sample. Applicant states on page 18 that Iwamoto et al.'s statement that expression profiling is one of the strongest methodologies to reveal the molecular basis of mental disorders supports applicant's position that the instantly claimed invention should be presumed enabled. However, in the quotation from the reference is not addressing the state of the art at the time the invention was made, nor is it stating that all expression results should be taken as being enabled for detection of disease. To the contrary, the reference discusses many limitations with expression analysis that existed years following the filing of the instant patent application and highlights the unpredictable nature of the technology area.

Applicant submits that the teachings of Tsuang et al. are clearly in favor of experimental data similar to that as disclosed as being reliable (p. 18), pointing to Tsuang et al. where they suggest that the work demonstrates the **potential** utility of blood-based RNA profiling in

diagnostics (emphasis mine). But Tsuang et al. specifically teach that to validate their results and overcome the limitations of sample size and inferential errors, their "approach must be extended to larger extensively characterized sample sets, and the convergence of several lines of evidence will ultimately determine the reliability and usefulness of the identified putative biomarker genes..." and that "future investigations will be performed on drug-naïve patients or their non-psychotic first-degree relatives (p. 4)." Tsuang et al. cannot be mistaken as suggesting that even the work they did was sufficient to establish the use of a single differentially expressed gene as sufficient to detect the presence of schizophrenia.

Regarding Vawter et al., applicant submits that the fold-change criterion according to which Vawter et al. teaches that a gene is differentially expressed is purely arbitrary and should not be interpreted as teaching that a p value is not sufficient to demonstrate differential expression, pointing out that even still, BTG2 does exceed the arbitrary value. This argument is not commensurate in scope with the claims which allow for any "statistically significant" difference or similarity to be indicative of disease.

The rejection is maintained and modified to address the amended claims.

Conclusion

4. No claim is allowed.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday, Tuesday, or Thursday, from 9:00 AM until 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached by calling (571) 272-0735.

The fax phone numbers for the organization where this application or proceeding is assigned are (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Juliet C. Switzer/
Primary Examiner
Art Unit 1634

October 17, 2007